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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,699	03/30/2001	Munehide Kano	50026/022002	7451

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,699	KANO ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,9,11-20,24,26,28-33,37,39,41-66* is/are pending in the application.

4a) Of the above claim(s) *46-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,9,11-20,24,26,28-33,37,39,41-45 and 62-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed 7/28/05 have been entered. Claims 1, 2, 5, 7, 9, 11, 16, 17, 20, 24, 33, 37, and 39 have been amended, and claims 62-66 are newly submitted.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 8/15/05 response would be addressed to the extent that they apply to current rejection.

Claims 1-5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-45, 62-66 are under current examination.

Claim Objections

Claims 12, 28, 41 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. These claims recite "gp41", however the previous claims from which they depend from do not embrace the gp41 protein. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-45 stand rejected and claims 62-66 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record and following.

Applicant asserted that pages 22-23 of the specification provides specific exemplary parts of a pol, gp41, tat, rev, vap, vpx vpr vif nef gag or gag-pol fusion protein, and unambiguously informs skilled artisans of the parts of these proteins.

In response, the applicant is reminded that the central issue under this rejection is the structure-functional relationship of the HIV/SIV proteins and the parts thereof, and whether the protein and the parts thereof have the capability of serving as a vaccine for HIV/SIV. As discussed previously, although it is known in the art that the HIV viral proteins could be cleaved and truncated to many parts (fragments), it is not fully developed and often controversial in the art concerning which parts of the protein has the capability to induce a meaningful and specific immune response against HIV/SIV to such extend that it becomes a vaccine. Moreover, it is noted that pages 22-23 of the specification provides discussion regarding exemplary parts of the gag and env proteins, but not the rest of the recited proteins, and it does not provide the teaching regarding the immunogeneicity of the HIV/SIV proteins and the discussed parts. Thus the specification fails to provide adequate written description on this matter, and thus fails to meet the requirement under this provision.

Turning to the publication of *Matano et al*, the applicant alleged that the Office misconstrued the Matano teaching, which teaches that a tat-specific immune response

was in fact induced though tat is less effective than Gag. In response, applicant's attention is directed to the 3rd paragraph of column 2, page 1392, where *Matano et al* teach a vaccine regimen comprising a DNA-prime followed by a SeV-Tat. They reported that in the group giving DNA-prime alone, all three animals showed lower setpoint viral loads and were protected from progression to AIDS , although one of them showed acute CD4 T cell depletion (the symptom of HIV/SIV); and the outcome was the same for the group giving DNA-prime followed by SeV-Tat boost. It is apparent SeV-tat failed to influence an anti-viral response since the same outcome was shown compared to the group giving DNA-prime alone. *Matano et al* did stated "THESE RESULT DO NOT DENY THE POTENTIAL OF TAT-BASED AIDS VACCINES", here the word "potential" is important because, at a post-filing date, they have yet to show that SeV-Tat is enabled to be an AIDS vaccine when it does not even enhance the response to a proven effective DNA-prime composition. *Matano et al* went on to teach, "BUT SUGGEST THE IMPORTANCE OF THE CAREFUL SELECTION OF ANTIGENS FOR THE DEVELOPMENT OF AN AIDS VACCINE" (paragraph bridging pages 1392-3, emphasis added). Such selection is apparently on a trial and error basis since there is no known consensus region that guarantee an effective anti-viral response. Accordingly, the teaching of *Matano et al* illustrated the state of the art and the levels of the skilled in the art, and implicitly indicated not every HIV/SIV or the fragment thereof could serve as an AIDS vaccine even at the time of a post-filing date.

It is noted *Matano et al* reviewed the state of the art concerning the development of the Tat-based AIDS vaccines, which presented mixed results, and concluded, "THE EFFICACIES OF TAT-BASED AIDS VACCINES MAY THUS BE DEPENDENT ON ANTIGEN-DELIVERY

SYSTEMS" (paragraph bridging columns 1-2, page 1392). This teaching is important because *Matano et al* have shown that with the SeV antigen-delivery system, Tat fails to serve as a SIV/HIV vaccine.

Therefore, for reasons of record and set forth *supra*, only the described V(-) SeV/SIV-Gag meets the written description provision of 35 U.S.C. §112, first paragraph.

Claims 1-5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-45, 62-66 stand or newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and set forth *supra*.

In view of the amendment, persuasive arguments supported by the newly submitted evidence, the previous rejection has been modified as following:

Claims 1, 3, 5, 7, 9, 20, 24, 26, 28, 30-33, 37, 39, 41, 43-45, 62-64 stand or newly rejected under 35 U.S.C. 112, first paragraph, because the specification supplemented by the state of the art, while being enabling for intranasally administering a sendai virus vector expressing a protein of an immunodeficiency virus selected from the group consisting of Gag, Pol, gp41, Gag-pol, does not reasonably provide enablement for obtaining a vaccine effect by intranasally administering a sendai viral vector expressing parts of the Gag, Pol, gp41, Gag-pol proteins, or expressing the tat, rev, vap, vpx vpr vif nef proteins, and parts thereof. The specification does not

reasonably provide enablement for encoding the genome of an immunodeficiency virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Concerning the type of immunodeficiency proteins, the applicant asserted the mere listing of the viral proteins constitutes a constructive reduction to practice of each member of the claimed genus, citing several art of record as support.

In response, in the presence of evidence to the contrary as presented on record and following, mere listing of the viral proteins is insufficient to support the full scope of the claimed invention. Here, those references not concerning Gag, gp41 env, and gag-pol proteins will be addressed below.

a. *Ensoli et al* teach tat protein immunization, cannot rely on as the sole support for genetic vaccination. Moreover, the reference fails to support the enablement of SeV-tat as a vaccine particularly in view of the *Matano* (AIDS 2003) reference as discussed previously and *supra*, and *Allen* (J Virol 2002, IDS) reference, which indicated despite the induction of tat-specific CTL, there was no significant reduction in either peak or viral set point compared to controls (e.g. abstract), and thus no protective effect on viral infection as should a vaccine.

b. *Leung et al* disclosed recombinant BCG expressing gag, pol, env and nef of SIV/HIV proteins. The reference does not support the use of SeV-nef as a vaccine because *Leung et al* combined the four BCG constructs in a single inoculum, and the results reflected the combined effect of the four, not nef alone (3rd paragraph, page 95).

Moreover, *Leung et al* only examined cellular and humoral immune responses induced, and did not teach whether such immune response is associated with a protective immune response, which is required for evaluating a vaccine. As indicated by numerous teaching in the field (e.g. *Allen* April 2002 and *Allen* Oct. 2002), including *Leung et al*, inducing an immune response, even a CTL response, often does not correlates with a protective effect for HIV/SIV viral infection (e.g. 2nd paragraph, page 95).

c. As with *Leung et al*, *Ayyavoo et al* made attenuated HIV-1 accessory gene expression construct, induced immune response *in vitro* and *in vivo*, but fails to teach such responses would lead to a protection on HIV/SIV viral infection.

d. *Ciernik et al* teach using an antigenic epitope for genetic tumor vaccine, they did not show that the epitope asserted any effect on HIV/SIV viral infection.

e. *Allen et al* (Oct. 2002) tested immunodominant gag epitope, which induced strong CTL response. Yet again, *Allen et al* reported, "BY THEMSELVES, THESE STRONG CTL RESPONSES FAILED TO CONTROL SIVMAC239 REPLICATION" (e.g. abstract), this illustrated the dissociation between the immune response induced by the HIV/SIV proteins and the vaccination.

Allen et al cannot be used to support the parts of the gag protein, also because it was published after the effective filing date, and the parts was not available at the time of the instant priority date.

f. *Allen et al* (April 2002) teach Tat-based vaccine does not control SIV replication, yet again pointing to the non-enablement of instantly claimed invention.

g. *Subbramanian* (Sep 2003) reference cannot be used to support the parts of the gag protein, because it was published after the effective filing date, and the parts was not available at the time of the instant priority date, nor any epitope was taught by the instant disclosure.

Accordingly, for reasons of record and set forth *supra*, the specification fails to provide adequate support to enable the full scope of instant claims, and the rejection stands.

Applicant fails to address the concerns regarding genomic DNA of immunodeficiency virus as indicated in page 15 of the Office action mailed on 1/26/05. Thus, for reasons of record, the rejection stands.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 16-19 stand rejected under 35 U.S.C. 103(a) as being obvious over *Nagai et al* (US application 09/728,207, now allowed), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hirsch et al* (J Virol 1996;3741-52).

Applicants indicated they would address this rejection upon an indication of allowable subject matter. Until then, the rejection stands for reasons of record.

Previous rejection has been modified to include claims 4 and 19 in view of the amendment of claims 2 and 17.

Claims 1-5, 7, 9, 16-20, 24, 26, 28-33, 37, 39, 41-45, 62-66 stand or newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), *Seth et al* (PNAS 1998;95:10112), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hurwitz et al* (Vaccine 1997;15:533-40); and as evidenced by *Ourmanov et al* (J Virol 2000;74:2740-51, IDS), for reasons of record and following.

Majority of the arguments in the 8/15/05 response have been addressed in the previous Office action mailed 1/26/05, and thus will not be reiterated here. The new arguments will be addressed below.

Applicants asserted that Kast reference casts doubt on the ability of wild-type sendai virus to ubiquitously induce a specific CTL response to sendai viral proteins themselves, noting the example of the bm14 mouse. In response, *Kast et al* clearly teach the lack of response in bm1 mice is caused by the defect in antigen presentation by dendritic cells, possibly due to the mutation in H-2K^b, and pointing to the fact that virus-infected DC can overcome the defect (last paragraph of page 3186). Accordingly, *Kast* reference does not cast double on the ability of wild-type sendai virus but illustrating the influence of dendritic cells and antigen-presentation process.

Applicant then asserted that Yu reference casts doubt on the ability of the Sendai virus to express foreign proteins other than gp120 noting the recorded failure to yield functional luciferase. In response, contrary to applicant's interpretation, *Yu et al* clearly

teach, "HERE, A FOREIGN GENE WITH SEV SPECIFIC E AND S SIGNALS CAN BE READILY INSERTED BY THE AID OF A NEWLY CREATED UNIQUE NOTI SITE IN THE VIRAL CDNA. ANOTHER UNIQUE SITE CAN, IN PRINCIPLE, BE CREATED AT THE SAME POSITION WITHOUT DISTURBING VIRAL REPLICATION". And concluded "THUS, ANY GENE TAGGED ACCORDINGLY WILL BE REAILY INSERTED INTO SEV OR V(-)SEV IN A SINGLE-STEP, CASSETTE-LIKE FASHION" (column 2, page 463). As to the luciferase, the problem in assessment appears not in the failure to yield functional luciferase, but over-production lead to "EXTENSIVE AGGREGATION OF THE EXPRESSED LUCIFEREASE MOLECULES IN CELLS" (emphasis added).

Accordingly, for reasons of record and set forth *supra*, the rejection stands.

Claims 11-13 and 15 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS), for reasons of record and *supra*.

Claim 14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS) as applied to claims 11-13, and 15 above, further in view of *Boutillon et al* (US 6,015,564), for reasons of record and *supra*.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 16-19 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 5, 13 of copending Application No. 09/728,207, now allowed, in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hirsch et al* (J Virol 1996;3741-52), for reasons of record.

No response was presented to this rejection in the Remark filed 7/28/05/05

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave T. Nguyen** can be reached on 571-272-0731. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Victor Barlow**, whose telephone number is (571) 272-0506.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is **(866) 217-9197**. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within

5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
October 20, 2005